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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/729,468	12/04/2000	J. Clifford Waldrep	D6288	4457

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EXAMINER

HAGHIGHATIAN, MINA

ART UNIT PAPER NUMBER

1616

DATE MAILED: 01/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/729,468

Applicant(s)

WALDREP ET AL.

Examiner

Mina Haghighatian

Art Unit

1619

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8, 14, 15 and 17-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4 is/are allowed.
- 6) ☒ Claim(s) 1-3, 5, 6, 8, 14-15 and 17-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 December 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3. 6) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 3, 6 and 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Densmore, Jr. et al (6,106,859).

'859 teaches a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, a neutral composition-lipid and a tryptone. '859 discloses the use of 5% carbon dioxide in aerosolized preparations for enhancing the deep breathing of animals and thereby enhancing the lung deposition of the transfection formulations. The animal is exposed to aerosol for a period of 1 minute (col. 2, lines 20-26).

Also disclosed is that animals were subjected to either intermittent aerosol exposure of the lipid:DNA (chloramphenicol acetyl transferase) formulations indicated, using a jet nebulizer, for 1 minute of aerosol followed by a 9 minute delay to allow the animals breathe the aerosol (col. 2, lines 55-67).

'859 teaches that the pharmaceutical compound is a gene in the form of plasmid DNA. Representative examples of useful phospholipids include phosphatidylcholine, dimyristoylphosphatidylcholine, dilaurylphosphatylcholine, dioleoyl-phosphotidylethanolamine (col.3, lines 18-37).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 17-18 and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Densmore, Jr. et al as applied to claims 3, 6 and 19-22 above, and in view of Knight et al (6,090,407).

Densmore was discussed above, however it lacks teachings on drugs such as the anti-cancers.

Knight et al teaches small particle liposome or lipid complex aerosol compounds and methods of treatment, which involves lipid or water soluble anti-cancer drugs incorporated into liposomes or other lipid complexes. The liposomes and complexes Are administered in aqueous dispersions from a jet nebulizer to the respiratory tract of an individual. Various anti-cancer drugs may be used, including Camptothecin, Taxol and their derivatives (see abstract and col. 5, lines 38-40).

Knight discloses that if the drug is water soluble, it may be incorporated by appropriate procedures in aqueous vesicles in lipids, and if the drug is lipid soluble, it will associate with the lipid molecules in a manner specific to the lipid employed (col. 1, lines 12-39).

It would have been obvious to a person of ordinary skill at the time the invention was made to have modified the process of using carbon dioxide in aerosolized compositions as taught by Densmore, by adding the anti-cancer medications in an aerosol formation, as taught by Knight, with a reasonable expectations of obtaining an aerosolized composition for cancer treatment which enhances lung deposition of the actives.

Claim 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Densmore, Jr. et al as applied to claims 3, 6 and 19-22 above, and further in view of Waldrep et al (5,958,378).

Densmore's teachings, discussed above, fail to disclose some drugs useful for aerosol compositions.

Waldrep teaches high dose pharmaceutical liposome aerosol compositions. The active agents are those such as anti-inflammatory glucocorticoids, immunosuppressive compounds, antifungal compounds, antibiotics, anti-virals, and anti-cancer compounds delivered via a high dose liposome aerosol composition in a phospholipid (see abstract).

It would have been obvious to a person of ordinary skill at the time the invention was made to have modified the process of using carbon dioxide in aerosolized compositions as taught by Densmore, by adding the compositions of Waldrep containing various classes of medications such as antibiotics, anti-virals, anti-cancer, etc, in an aerosol formation, with a reasonable expectations of obtaining an aerosolized composition for variety of treatments, which enhances lung deposition of the pharmaceutical actives.

Claims 14-15 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Densmore Jr. et al as applied to claims 3, 6 and 19-22 above, and further in view of Kim et al (International Journal of Pharmaceutical).

Densmore was discussed above, however it lacks specific teachings on modified liposomes.

Kim et al teaches pharmacodynamics of insulin in polyethylene glycol-coated liposomes. Kim et al reads "in this study, to evaluate liposomes as safe and sustained injectable delivery systems of proteins, we chose insulin as a model protein drug and tested its incorporation efficiency and pharmacodynamics in various liposomes with and without polyethylene glycol (PEG)-derivatized phospholipid. The liposomes coated with PEG showed 3-fold higher efficiency of insulin incorporation than did the liposomes without PEG. Moreover, among the liposomes coated with PEG, dipalmitoylphosphocholine (DPPC) liposomes showed higher incorporation efficiency than did dimyristoylphosphocholine (DMPC) liposomes" (see abstract, lines 1-7).

Kim concludes that of various liposomes, PEG-coated DPPC liposomes might have advantages over other liposomes, based on the higher incorporation efficiency, narrow size distribution and stability in vitro and in vivo. Also suggested that PEG-coated liposomes might be further developed as safe and sustained injectable delivery systems of other peptide and protein drugs (page 80, column 2, item 4).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of phospholipids in drug delivery systems to have looked in the art for a more specific phospholipid (or modifications) as taught by Kim et al, to prepare a composition with higher efficiency and stability.

Allowable Subject Matter

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Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

The upper carbon dioxide limitation of claim 4 is not taught by the prior art.

Response to Arguments

The rejection of claims 1-24 under 35 U.S.C. 112, second paragraph are withdrawn in light of the amendments.

The rejection of claim 1 under 35 U.S.C. 102 (e), and the rejection of claim 4 under 35 U.S.C. 103 (a) is withdrawn in light of the amendments and remarks.

Claims 1-3, 5, 6, 8, 14-15 and 17-24 stand rejected as discussed above. Claims 7, 9-13 and 16 are canceled.

Applicant's arguments filed 12/07/2001 have been fully considered but they are not persuasive. The prior art does not teach the higher limitation of carbon dioxide in the claimed composition for administration by aerosol, however it does teach and suggest the lower limitations of carbon dioxide and the method of delivering the composition and the particles to the lung as claimed by the applicant. In light of the amendments, Densmore '859 is no longer considered prior art under 35 USC 102 (e) for claim 1, however it is meeting claims 3, 6 and 19-22 and is considered prior art under 35 USC 103 for claims ¹2, 5, 8, 14-15, 17-19 and 23-24.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghghatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

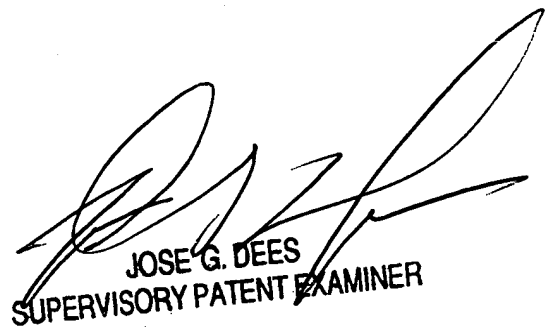
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached at 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.



Mina Haghghatian

January 28, 2002



JOSE G. DEES
SUPERVISORY PATENT EXAMINER

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